A COMPARATIVE STUDY OF TWO DOSES OF INTRATHECAL CLONIDINE WITH BUPIVACAINE IN INGUINAL HERNIA SURGERIES

A STUDY OF 90 CASES

DISSERTATION SUBMITTED FOR THE DEGREE OF

DOCTOR OF MEDICINE

BRANCH – X (ANAESTHESIOLOGY)

MARCH - 2010

THE TAMILNADU
DR. M.G.R. MEDICAL UNIVERSITY
CHENNAI, TAMILNADU

BONAFIDE CERTIFICATE

This is to certify that this dissertation entitled **"A COMPARATIVE STUDY OF TWO DOSES OF INTRATHECAL CLONIDINE WITH BUPIVACAINE IN INGUINAL HERNIA SURGERIES"** is bonafide record work done by **Dr. T. JAYAPRAKASH** under my direct supervision and guidance, submitted to the Tamil Nadu Dr. M.G.R. Medical University in partial fulfillment of University regulation for MD, Branch X –Anaesthesiology.

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DECLARATION

I **Dr.T. JAYAPRAKASH** solemnly declare that this dissertation titled **"A COMPARATIVE STUDY OF TWO DOSES OF INTRATHECAL CLONIDINE WITH BUPIVACAINE IN INGUINAL HERNIA SURGERIES"** has been done by me. I also declare that this bonafide work or a part of this work was not submitted by me or any other for any award, degree, diploma to any other University board either in India or abroad.

This is submitted to The Tamilnadu Dr. M. G. R. Medical University, Chennai in partial fulfillment of the rules and regulation for the award of Doctor of Medicine degree Branch –X (Anaesthesiology) to be held in March 2010.

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ACKNOWLEDGEMENT

I am greatly indebted to **Dr. I.CHANDRASEKARAN, M.D., D.A,** Professor and Head of the Department of Anaesthesiology, Madurai Medical College, Madurai for his guidance and encouragement in preparing this dissertation.

My sincere thanks to **Dr. SP. Meenakshi Sundaram, M.D., D.A,** Additional Professor of Anaesthesiology, Madurai Medical College, Madurai for his able assistance in completing this study.

My heartful thanks to **Dr. S.C.GANESH PRABHU, M.D., D.A,** Additional Professor of Anaesthesiology, Madurai Medical College, Madurai for his guidance in doing this work.

I also thank my Additional Professors **Dr. T. THIRUNAVUKARASU, M.D., D.A,** and **Dr.P.SHANMUGHAM M.D., DCH.,** for their constant support and guidance in performing this study.

I also thank my Assistant Professor **Dr.G.K.KUMAR, MD., D.A** for her constant support in conducting this study.

My profound thanks **Dean**, Madurai Medical College and Government Rajaji Hospital, Madurai for permitting to utilize the clinical materials of this hospital in the completion of my dissertation.

I gratefully acknowledge the patients who give their consent and co-operation for this study.

TABLE OF CONTENTS

INTRODUCTION

"It is the duty of the anaesthesiologist to study the well being of the patient as well as the convenience of the surgeon"

-R.M.WATERS

"The proper dose of any drug is enough"

– THOMAS SYDENHAM

The anaesthesiologist chooses a drug or mixture of drugs that best fits the anticipated needs of the operation and as laycock in 1953 has written "Reflexes are his essential guides in this matter. He must understand them, look out for them, nurse them, leave them alone, depress or abolish them"

- WYLIE

"It is not the drug that is dangerous, but the man who administers it is"

- SIR ROBERT MACINTOSH

Cerebrospinal fluid discovered by Domenico cotungo in 1764 and its circulation described by F.Magendie in 1825. First spinal analgesia by J.Leonard corning in 1885. He accidentally pierced the dura while experimenting with cocaine on the spinal nerves of the dog. Later he deliberately repeated the intradural injection, called it spinal anaesthesia and suggested it might be used in surgery.

First planned spinal analgesia for surgery in man performed by August Bier on 16th august 1898, in kiel when he injected 3 ml of 0.5 % cocaine solution into a 34 year old labourer.

For inguinal hernia surgeries, the standard anaesthetic technique is subarachnoid block. Adrenaline being the first spinal adjuvant used to increase the duration and to reduce the toxicity of spinal anaesthesia in 1903. From then many drugs have been tried in search for an ideal adjuvant. They are opioids, soda bicarbonate, ketamine, neostigmine, midazolam and the latest inclusion is clonidine.

ADVANTAGES:

Initially opioids have been the standard choice as spinal adjuvants. But since there occurs many side effects and complications like early and late depression of ventilation , pruritus, nausea, vomiting, urinary retention, central nervous system excitation, viral re activation, sexual dysfunction, delayed gastric emptying, ocular dysfunction, there is an active search for an alternative ideal adjuvant which is devoid of these side effects and complications.

Preservative free clonidine when administered into epidural or subarachnoid space produce dose dependent analgesia and unlike opioids does not produce any of its side effects. Activation of post synaptic

alpha 2 receptors in the substantia gelatinosa of the spinal cord is the presumed mechanism by which it produces analgesia.

Clonidine at appropriate doses when used as an adjuvant with bupivacaine in subarachnoid block seems to prolong the duration of surgical anaesthesia and postoperative analgesia without any of its side effects like dry mouth, hypotension, bradycardia, which is not usual in these doses with added advantages like sedation, anti- shivering.

This study has been taken in search for a minimal dose of clonidine as an adjuvant with bupivacaine which produces maximum post operative analgesia without or with minimal incidence of its side effects.

AIM OF THE STUDY

The aim of this study is to evaluate the duration of post operative analgesia provided by two varying doses of clonidine with bupivacaine against bupivacaine alone in subarachnoid blockade in inguinal hernia surgeries.

ANATOMY OF SUBARACHNOID SPACE

Subarachnoid block means the temporary interruption of nerve transmission within the subarachnoid space produced by injection of a local anaesthetic solution into cerebrospinal fluid.

Applied anatomy of vertebral canal:

Vertebral canal extends from foramen magnum to the sacral hiatus. It protects the spinal cord.

The vertebral column comprised 33 vertebrae (7-cervical, 12-thoracic, 5-lumbar, 5-fused sacral and 4-coccygeal) and four curves. Cervical and lumbar curves are convex anteriorly and thoracic & sacral curves are convex posteriorly. The curves of the vertebral column influences the spread of the local anaesthetic in the subarachnoid space.

Each vertebra is composed of a body separated from the adjacent vertebra by intervertebral disc and formed by pedicles and laminae, which surround and protect the cord laterally and posteriosly.

The vertebral column is bound together by several ligaments. They are,

1. Supraspinous ligament – passes longitudinally over the tips of the spinous processes from C7 to the sacrum.

2. Interspinous ligament – connects the adjoining spinous processes together.
3. Ligamentum Flavum – known as yellow ligament, connects the adjacent laminae composed of yellow elastic fibres. They become progressively thicker from above downwards.
4. Posterior longitudinal ligament – It is on the posterior surface of bodies of vertebra.
5. Anterior longitudinal ligament – It runs along the front of the vertebral bodies.

There are seven projections from these vertebral (or) neural arches. They are,

a) Three muscular processes – (2-Transverse processes, 1-spinous process for the attachment of muscle and ligaments).
b) Four articular process – Two upper & two lower which in the lumbar region prevent rotation but allow limited flexion and extension between contiguous vertebrae.

Vertebral canal formed by these structures has deficiencies posteriorly in the midline called inter laminar foramina which enlarge in flexion accessible for the passage of spinal needle. The direction of spinous process determine the direction of spinal needle.

SPINAL CORD:

It is the direct continuation of the medulla oblongata extending from the upper border of the atlas to the first lumber vertebra below which there is leash of nerve roots termed cauda equina. Spinal nerves are 31 pairs totally.

8 – Cervical

12 – Thoracic

5 – Lumbar

5 – Sacral

1 – Coccygeal

Each of the spinal nerve is composed of anterior and posterior roots uniting at the intervertebral foramina and form a nerve trunk. Membranes covering the spinal cord from without are dura mater, arachnoid mater and piamater. Dura and arachnoidmater ends at S_2 level. Piamater is closely applied to the spinal cord.

BLOOD SUPPLY:

It is from the anterior spinal artery which is a branch of vertebral artery and also by a pair of posterior spinal arteries which arise from the posterior inferior cerebellar arteries. There is no anastamosis between these arteries.

SPINAL VEINS:

The spinal veins are arranged into anterior and posterior plexus which are draining into vertebral, azygos and lumbar veins.

CEREBROSPINAL FLUID:

This is an ultrafiltrate of the blood plasma from choroids plexus of the lateral ventricles with a pH of 7.32 (7.27-7.37)

It is a clear, colourless fluid found in the cranial and spinal subarachnoid space and in the ventricle of the brain. The total volume of CSF in an average adult ranges from 120-150ml of which 25-35ml is in the spinal subarachnoid space.

Composition of cerebrospinal fluid:

Specific gravity	-	1.006 (1.003-1.009) at 37^0C
Pressure	-	60-80mm of water
Pco_2	-	48mmHg
Bicarbonate	-	23meq/l
Sodium	-	133-145meq/l
Calcium	-	2-3meq/l
Phosphate	-	1.6mg/dl
Magnesium	-	2-2.5mg/l
Chloride	-	15-20meq/l
Protein	-	23-38mg/dl
Sugar	-	45-80mg/dl
Lymphocytes	-	0-5cells/cmm

An important factor that determine the spread of drug in cerebrospinal fluid is the baricity of the solution. Baricity is the density of the solution in relation to cerebrospinal fluid. The density of the solution is the mass of drug (gram) per ml of the solution.

PHYSIOLOGY OF SUBARACHNOID BLOCK

Subarachnoid block implies the temporary interruption of nerve transmission within the subarachnoid space by injection of local anaesthetics. The blockade of nerve fibres occur in the order of Temperature, Pain, proprioceptive and then motor fibres.

FACTORS INFLUENCING BLOCK HEIGHT:

a - Site of injection

b - Angulation of needle

c - Characteristic of local anaesthetic- baricity

d - Dose of local anaesthetic

e - Position of the patient during and after injection

f - Anatomic configuration of spinal column.

g - Patient height (at extremes)

h - Volume of cerebrospinal fluid

i - Reduced cerebrospinal fluid with increased intra abdominal pressure (eg. Pregnancy)

a) Effects on Cardio Vascular System:

Most important physiological responses to subarachnoid block involve cardiovascular system due to combined effect of autonomic denervation, higher level of neural block, added effect of vagal innervation.

Local anaesthetics and vasoactive substances administered in small doses intrathercally leads to direct cardiovascular effect.

Level of sympathetic denervation determines the magnitude of cardiovascular system responses, but the relationship is neither predictable nor precise.

Sympathetic denervation produces arterial and more physiologically important arteriolar dilatation and vasodilatation in the venous circulation produces fall in blood pressure.

Due to Bainbridge reflex, the fall in blood pressure is associated with bradycardia, blockade of cardiac sympathetic fibres from T1-T4 is an additional factor that causes bradycardia.

b) Effects on Respiratory System:

Respiration is not depressed normally. High spinal can cause paralysis of intercostal muscles but the resting tidal volume, maximum inspiratory volume, respiratory rate, negative intrapleural pressure and also

the phrenic nerve are unaffected. Hypoxia may accompany hypotension and is corrected by oxygen administration via face mask.

c) Gastro Intestinal Effect:

Preganglionic fibres from T_5-L_1 are inhibitory to gut. So in sympathetic blockade the small intestine contracts with relaxed sphincters and peristalsis remains normal. Handling of viscera causes discomfort and bradycardia since vagus is not blocked.

d) Hepatic and Renal Effects:

The hepatic blood flow decreases and is directly proportional to the decrease in blood pressure. There may be normal hepatic oxygen extraction. Renal blood flow is maintained by autoregulation and does not decrease till mean arterial pressure goes below 50mmHg.

e) Genito Urinary System:

Sphincters of bladder are not relaxed, and the ureteric tone are not greatly altered. Urinary retention occurs. Penis is often engorged. Uterine tone is unchanged in pregnancy. In the absence of hypotension spinal anaesthesia has got no effect on the progress of labour and uterine blood flow.

f) Metabolic and hormonal effect:

Spinal anaesthesia blocks the hormonal and metabolic responses to nociceptive stimuli arising from the operative site. It minimizes the rise in

blood sugar, coritsol, catecholamines renin and aldosterone release associated with stress. Post operative negative nitrogen balance and secretion of antidiuretic hormone are inhibited.

g) Thermo Regulation:

Hypothermia results from heat loss to the cold environment due to vasodilatation.

INGUINAL HERNIA SURGERIES:

Among the infraumbilical surgeries inguinal hernia surgeries stands one of the commonest indications in adults. Its a protrusion of abdominal content, omentum through the superficial inguinal ring. The usual mode of anaesthetic plan is subarachnoid block. And if it is strangulated , combined epidural spinal blockade or general anaesthesia sometimes are the techniques since resection anastamosis may be done .

It may be a bubonocoele, incomplete or complete hernia. According to its site of exit it may be indirect or direct hernia. According to contents it may be enterocele, epiplocele, cystocele. Also it may be reducible, irreducible, obstructed (incarcerated), strangulated and inflammed hernia.

PHARMACOLOGY OF DRUGS

a) Bupivacaine:

Bupivacaine is an amide linked local anaesthetic. It is a hydrochloride salt of 1-butyl-N-(2, 6-dimethylphenyl) piperidine-2-carboxamide and is presented as a racemic mixture.

- It was synthesized by Ekenstem in 1957.
- First reports of its use was published in 1963 by Telivuo.
- It is derived from Mepivacaine and is very stable compound and may be autoclaved repeatedly.

Pka is 8.1

Molecular weight	-	288
Protein binding	-	95%
Lipid solubility	-	28
Elimination half life	-	210mts
Toxic plasma concentration	-	>1.5µg/ml
Approximate duration of action	-	175mts

Availability:

Ampoules - 0.5% Bupivacaine hydrochloride 4cc

- 0.5% Bupivacaine hydrochloride with dextrose (heavy) 4cc

Vials - 0.25% and 0.5% Bupivacaine hydrochloride 20cc

Dosage - Maximum dosage 3mg/kg body weight.

Uses:

- Spinal anaesthesia
- Epidural anaesthesia
- Caudal anaesthesia
- Continuous epidural anaesthesia
- Peripheral nerve block

Onset time and duration of action

Site of action	Onset (minutes)	Duration (minutes)
Intrathecal	5	90-120
Epidural	15-20	165-225
Brachial plexus	10-20	600

Pharmacokinetics:

Once injected intrathecally, it gets absorbed by the nerve rootlets and results in the desired effect. It is rapidly absorbed from the site of injection, but the rate of absorption depends on the vascularity at the site and the presence of vasoconstrictors.

High lipid solubility of bupivacaine makes it easy for nerve and vascular tissue penetration.

80-95% of the absorbed bupivacaive binds to the plasma proteins.

Distribution:

Rapid distribution phase: (α)

In this phase the drug is distributed to highly vascular region $t1/_2$ of α - being 2.7 minutes.

Slow disappearance phase: (β)

In this phase the drug distributes to slowly equilibrating tissues $t1/_2$ of β – being 28mts.

Biotransformation and excretion phase δ

$T1/_2$ of δ is 3.5hours clearance is 0.47 litre/minute.

Biotransformation:

Possible pathways of metabolism of bupivacaine include aromatic hydroxylation and conjugation. Only the N-dealkylated metabolite, N-desbutyl bupivacaine has been measured in blood (or) urine after epidural (or) spinal anaesthesia. Alpha1 acid glycoprotein is the most important plasma protein binding site of bupivacaine and its concentration is increased by many clinical situations including post operative trauma.

Excretion:

It is through the kidney, 4-10% of the drug is excreted unchanged.

Mode of Action:

a) Site of action:

i) The spinal nerve rootlet fine nerve filaments having a large surface area are exposed to the local anaesthetics.

ii) Posterior and lateral aspects of the spinal cord itself.

b) Sodium Channel blockade:

They impede sodium ion access to the axon interior by occluding the transmembrane sodium channels thus delaying the process of depolarization and axon remains polarized. It is a non-depolarisation blockade.

Pharmacodynamics:

It has got a longer duration of action but a slower onset.

Cardiovascular system:

It reduces cardiac output by reducing the sympathetic tone, by slowing the heart rate and by reducing the venous return, it produces a fall in arterial blood pressure but it is relatively slow and is seldom very profound.

It produces a fall in central venous pressure. It causes an increase in lower limb blood flow. It causes a reduction in incidence of deep vein thrombosis.

Respiratory System:

It relaxes bronchial smooth muscle. Apnea can results from phrenic and intercostal nerve paralysis or depression of the medullary respiratory center following direct exposure to drug.

Gastro intestinal tract:

There is an increase in gastro intestinal motility and emptying of the gastric contents are better.

Toxicity:

Toxicity is related to plasma level of unbound drug and more likely due to an inadverdant intravenous injection. Systemic toxicity reactions primarily involve central nervous system and cardio vascular system. The blood level required to produce central nervous system toxicity is less than that required to produce circulatory collapse.

Central Nervous System Toxicity:

Early symptoms are circumoral numbness, tongue paresthesia, and dizziness. Sensory complaints include tinnitus and blurred vision. Excitatory signs (restlessness, agitation, nervousness,paranoia) often precede central nervous system depression (slurred speech, drowsiness, unconsciousness). Muscle twitching heralds the onset of tonic clonic seizures. Respiratory arrest often follows. The excitatory reactions are the result of selective blockade of inhibitory pathways.

Cardiovascular System Toxicity:

The rate of depolarization in fast conducting tissue of purkinje fibres and ventricular muscle is decreased. The rate of recovery of bupivacaine induced block is slower than that of lignocaine.

Extremely high concentration of the drug causes sinus bradycardia, hypotension, atrioventricular heart block, idioventricular rhythms, and life threatening arrhythmias such as ventricular tachycardia, ventricular fibrillation and cardiac arrest.

PHARMACOLOGY OF CLONIDINE HYDROCHLORIDE

Introduction:

Clonidine hydrochloride is a centrally acting selective partial alpha -2 agonist introduced in early 1960s, it was during its use as a nasal decongestant that its anti- hypertensive property was found out. Subsequently more insights into the pharmacological properties has led to its use in clinical anaesthesia practice as well.

Clonidine hydrochloride is an imidazoline compound and exists as a mesomeric compound. The chemical name is 2-(2,6-dichlorophenylamino)-2-imidazoline hydrochloride. The structural formula is C9H9C12N3HCl.

The molecular weight is 266.56. Clonidine is an odourless, bitter, white, crystalline substance, soluble in alcohol and water. Clonidine improves the quality of anaesthesia, provides a more stable cardiovascular course during anaesthesia, presumably because of their sympatholytic effect and need for lower dose of cardioactive anaesthetic and reduces the dose requirement of the anaesthetic agent. Clonidine may reduce the halothane MAC by upto 50% in a dose dependent manner. Clonidine potentiates the anaesthetic action of the local anaesthetics with fewer side effects in peripheral nerve blocks and central neuraxial blockade.

Availability:

Available as one ml ampoule containing 150 micrograms.It should be stored below 25^{o}c.

Mechanism of action:

Clonidine is a centrally acting selective partial α2 adrenergic agonist with a selectivity ratio of 220: 1 in favour of α2 receptors. The three subtypes of α2 receptors are α2a, α2b, α2c. α2a receptors mediate sedation, analgesia, sympatholysis . α2b receptors mediate vasoconstriction and anti- shivering. The startle response may reflect the activation of α2c receptors. The drug is lipid soluble, penetrates the blood brain barrier to reach the hypothalamus and medulla when injected epidurally. It stimulates the inhibitory α2 adrenoreceptors to reduce the central neural transmission in the spinal neurons. Inhibition of substance- P release is believed to be involved in the analgesic effect.

The α2 adrenoreceptors are located on the afferent terminals of both peripheral and spinal neurons in the superficial laminae of the spinal cord and within several brain stem nuclei implicated in analgesia. The superficial laminae contain three groups of neurons: tonic, adapting, single- spike firing, all of which receive their primary

sensory input from Aδ and C fibres. Clonidine inhibits voltage gated Na+ and K+ channels and suppresses the generation of action potentials in tonic- firing spinal dorsal horn neurons, contributing to analgesic effect. The ability of clonidine to modify the function of potassium channels in the CNS (cell membrane become hyperpolarized) may be mechanism for profound decrease in anaesthetic requirements.

Another contribution to analgesic effect may be through the release of acetylcholine in the neuraxial region. The α2 adrenergic agonists also enhance analgesia from intraspinal opioids. Sedation is produced by its action on locus ceruleus.

Clonidine affects the blood pressure in a complex fashion after neuraxial or systemic administration because of opposing action at multiple sites. In the nucleus tractus solitarius and locus ceruleus of the brain stem, activation of post- synaptic α2 adrenoreceptors reduces sympathetic drive. It also activates nor-adrenergic imidazoline preferring binding sites in the lateral reticular nucleus producing hypotension and anti- arrythmogenic action. In the periphery it acts on pre-synaptic α2 adrenoreceptors at sympathetic terminals reduces the release of nor-epinephrine causing

vasorelaxation and reduced chronotropic drive. The brainstem and the peripheral effects of α2 adrenoreceptor stimulation are counterbalanced by the direct peripheral vasoconstriction through its action on α2 adrenoreceptors from the circulating concentrations of clonidine.

Sedation is a desired property. Clonidine produces a dose dependent sedation at the dose of 50 mics or more in less than 20 minutes regardless of the route of administration.

Clonidine doesn't induce profound respiratory depression even after massive overdose nor do they potentiate respiratory depression from opioids.

In peripheral nerves it produces a minor degree of blockade at high concentrations with some preference for C- fibres in the peripheral nerves and this effect in part enhance the peripheral nerve block when added to local anaesthetics, probably because the α2adrenoreceptors are lacking on the axons of peripheral nerves.

Pharmacokinetics;

Clonidine is well absorbed orally and is nearly 100% bio available and reaches peak plasma concentration within 60 to 90 minutes. The mean half life of the drug in plasma is about 9 to 12

hours, with approximately 50% metabolized in the liver whereas is it is excreted in an unchanged form by the kidney, and its half- life can dramatically increase in the presence of impaired renal function.

A transdermal delivery system is available in which the drug is released at a constant rate for about a week. Three or four days are required to achieve steady state concentration.

Clonidine is highly lipid soluble and readily distributes into extra- vascular sites including the central nervous system.

300 micrograms intravenously over 10 min produces:

Distribution t ½	:	11 ± 9 minutes.
Elimination t½	:	9 ± 2 hour, 41 hours in severe Renal dysfunction.
Volume of distribution	:	2.1 ± 0.4 l/kg
Plasma protein binding	:	20-40 % in vitro.
Metabolism	:	minor pathways with the major Metabolite, p- hydroxyclonidine.

Excretion:

70% of the dose, mainly in the form of unchanged parent drug (40-60%) in urine.

So, the elimination t1/2 of clonidine varies as a function of

creatinine clearance. In subjects undergoing hemodialysis only 5% of the body clonidine store was removed.

Dosage regimen;

Oral	-	3-5 μg/kg
Intramuscular	-	2 μg/kg
Intravenous	-	1-3 μg/kg
Epidural	-	1-2 μg/kg
Transdermal	-	0.1- 0.3 mg released per day

Precautions:

1. In patients with renal insufficiency, lower dose is needed.
2. Sudden withdrawal of prolonged continuous epidural infusion produces hypertensive crisis. So it should be gradually discontinued over 2 to 4 days.
3. Use with caution in patients with cerebrovascular or coronary insufficiency.
4. If a patient with beta blocker is on continuous epidural therapy, beta blocker should be withdrawn several days before discontinuation of epidural clonidine.
5. Intrathecal / epidural clonidine often causes bradycardia that if symptomatic can be treated with inj. Atropine.

Contraindications:

1. Known hypersensitivity to clonidine or components of the product.
2. In patients with brady arrhythmia or AV block.
3. Patients with severe cardiovascular disease
4. Patients with cardiovascular / hemodynamic instability.

Interactions:

1. Clonidine may potentiate the CNS- depressive effect of alcohol, barbiturates or other sedative drugs.
2. Narcotics may potentiate the hypotensive effects of clonidine.
3. Tricyclic anti depressants may antagonize the hypotensive effects of clonidine.
4. Concomitant administration of drugs with a negative chronotropic/ dromotropic effect (beta blockers, digoxin) can cause or potentiate bradycardiac rhythm disturbances.
5. Beta blockers may potentiate the hypertensive response seen with clonidine withdrawal.
6. Epidural clonidine may prolong the duration of pharmacologic effects of epidural local anaesthetics, opioids, neostigmine and other drugs.

USES:

1. Preanaesthetic Medication;

   Oral clonidine Preanaesthetic medication (5 μg/kg) (a) blunts reflex tachycardia associated with direct laryngoscopy for intubation of trachea, (b) decrease intraoperative lability of blood pressure and heart rate, (c) decrease plasma catecholamine concentrations, and (d) dramatically decrease anaesthetic requirements for inhaled and injected drugs. Clonidine also attenuates the rise in intraocular pressure associates with laryngoscopy and intubation.

2. Epidural block: Clonidine as a sole agent or in combination with opioids or local anaesthetics to provide excellent analgesia in labour analgesia. Epidural clonidine is also indicated for the treatment intractable pain, which is unresponsive to maximum dose of oral or epidural opioid, as do patients with reflex sympathetic dystrophy, neuropathic pain.

3. Spinal anaesthesia: Clonidine combined with local anaesthetics improves the quality and duration of the block, minimize the tourniquet pain during lower limb surgery, and prevents shivering.

4. Caudal anaesthesia: clonidine combined with local anaesthetics increases the duration of anaesthesia and analgesia by 2 or 3 times without hemodynamic side effects. Dose 2-3 μg/kg
5. Peripheral nerve blocks: Clonidine prolongs the duration of anaesthesia and analgesia with local anaesthetics by two times in a dose of 75 to150 micro grams.
6. Bier's block: 150 microgram of clonidine enhances the tolerance of tourniquet
7. It is also used in intra articular analgesia.
8. Protection against perioperative myocardial ischemia; clonidine decreases myocardial ischemia, infarction and mortality following cardiovascular surgery.
9. Clonidine is used in the treatment of hypertensive crises
10. Diagnosis of pheochromocytoma; clonidine, 0.3 mg will decrease the plasma concentrations of catecholamine in normal patients but not in the presence of pheochromocytoma.
11. Treatment of shivering; Administration of clonidine, 75 μg IV stops shivering by inhibiting thermoregulatory control.
12. Treatment of opioid and alcohol withdrawal syndrome

Side effects :

1. The most common side effects are sedation and xerostomia.

2. Cardiovascular complaints are bradycardia, hypotension, and ECG abnormalities like sinusnode arrest, junctional bradycardia; high degree AV block and arrhythmia are reported rarely. Occasionally require treatment of bradycardia with I.V anticholinergics. Orthostatic hypotension occurs rarely.

3. Rebound hypertension; Abrupt discontinuation of clonidine can result in rebound hypertension as soon as 8 hours and as late as 36 hours after the last dose. Symptoms of nervousness, diaphoresis, headache, abdominal pain, and tachycardia often precede the actual increase in systemic blood pressure. Labetalol is useful in treatment of rebound hypertension.

4. Skin rashes are occurs frequently.

5. Impotence occurs occasionally.

Over dosage and treatment:

There is no specific antidote for clonidine overdosage. Supportive measures like atropine, ephedrine, and i.v fluids are enough.

Yohimbine partially reverses the analgesia and sedation but not the BP and heart rate changes produced by the epidural clonidine.

FUTURE IMPLICATIONS;

1. The new algorithm includes clonidine for neuropathic pain as a second line single drug option.
2. Intrathecal clonidine prevents neuropathic hyperalgesia , so may be able to minimize the sequelae of spinal cord injury and the research is going on.

REVIEW OF LITERATURE

1. (2003) anaesthesia analgesia, 2003;96;1496-503 **dobrydnjov I et al** have used 6 mg of 0.5% heavy bupivacaine with 15 µg vs 30 µg of clonidine for unilateral spinal anaesthesia in unilateral inguinal hernia surgeries and showed it have produced excellent post-op analgesia. They concluded that on adding clonidine 15 µg to 6 mg of hyperbaric bupivacaine increases the spread of analgesia, prolongs the time to first analgesic request, and decreases postoperative pain, compared with bupivacaine alone, during inguinal herniorrhaphy under spinal anesthesia and also it doesnot prolong the motor blockade when compared to 30 µg group.

2. (2007) Indian Journal of Anaesthesia. **B.S.Sethi et al** have studied the efficacy of low dose intrathecal clonidine as adjuvant to bupivacaine in gynaecological surgeries. They have added 1µg/kg of clonidine with 2.5 ml of bupivacaine vs plain bupivacaine. The duration of analgesia was 614 minutes (mean) in clonidine group when compared to 223 minutes (mean) in control group. Also the two segment regression time and the duration of motor blockade was significantly prolonged in clonidine group. They concluded that by adding clonidine, the post op analgesia is significantly prolonged

with an effect on sedation, heart rate and MAP which does not require any therapeutic intervention.

3. (1989) British journal of anaesthesia, 1989;63;1;93-96 **Bonnet et al** studied spinal clonidine 150µg as adjuvant with 2.5 mg bupivacaine in orthopaedic surgeries and proved that the combination was effective in preventing the tourniquet pain and effectively prolonging the post-op analgesia without any side effects.

4. (1993) British journal of anaesthesia, 1993;71;5;661-64 **Fogarty et al** compared spinal clonidine vs morphine with bupivacaine in patients undergoing total hip replacement surgeries. The duration of postoperative analgesia was 278 minutes in clonidine group when compared to 498 minutes in morphine group. They concluded that intrathecal clonidine prolonged the duration of spinal analgesia, but was markedly inferior to the intrathecal morphine in providing subsequent postoperative analgesia.

5. (1994) British journal of anaesthesia, 1994;73;5;628-33. **Grace et al** studied the co administration of pethidine 0.75 mg per kg and clonidine 75 µg with 0.5% bupivacaine in spinal anaesthesia for total hip replacement surgeries.they concluded that the combination does not offer any major advantages over conventional agents.

6. (1998) canadian journal of anaesthesia , 1998;45;8;735-40 **Monica brunschwiller et al** compared intraoperative anaesthetic and haemodynamic effects of clonidine-bupivacaine, morphine-bupivacaine and placebo-bupivacaine combinations during continuous spinal anaesthesia in knee replacement surgeries. They concluded that 0.15 mg clonidine but not 0.15 mg morphine prolonged surgical analgesia when added to 10 mg plain bupivacaine.

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10. (2004)anaesthesia analgesia, 2004;98;1460-66 **Michael j. peach et al** studied intrathecal fentanyl with morphine and varying doses of clonidine in cesarean surgeries for post-op analgesia. They have added fentanyl 15 µg with morphine, clonidine, or both morphine and clonidine for cesarean delivery. A dose-finding analysis showed similar postoperative efficacy and side effects for groups receiving morphine 100 µg with clonidine 60, 90, or 150 µg. A multimodal approach to postcesarean analgesia, using subarachnoid bupivacaine, fentanyl, morphine 100 µg, and clonidine 60 µg, improves pain relief compared with morphine 100 µg or clonidine 150 µg alone, but increases intraoperative sedation and may increase perioperative vomiting.

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12. (2006) british journal of anaesthesia, 97(3); 365-70 **Van tuiji et al** have studied the addition of intrathecal clonidine to hyperbaric bupivacaine on post-op pain and morphine requirements after cesarean section. They concluded that addition of 75 μg clonidine to hyperbaric bupivacaine 2.2 ml prolongs spinal analgesia and motor block after cesarean section and improves early analgesia without any clinically relevant maternal or neonatal side effects.

MATERIALS AND METHODS

After getting the ethical committee approval the study was conducted in 90 patients undergoing elective inguinal hernia surgeries. It was a double blinded study in which patients were randomly allocated into three groups A, B and C. After getting informed consent and explaining the procedure details to the patients, the anaesthetic technique was performed.

EXCLUSION CRITERIA:

- Patient refusal
- ASA III & IV patients
- Post spinal surgeries
- Spinal deformity
- H/o drug allergy

Preoperative preparation:

After routine preoperative assessment as for all elective surgery patients ,

Patients were randomly divided into three groups.

Group A

- Received Inj. 0.5% Bupivacaine 2.4 cc+
  0.2 cc Normal saline = 2.6 cc

Group B

- Received Inj. 0.5% Bupivacaine 2.4 cc +
  Inj.Clonidine 15µg+ normal saline 0.1cc = 2.6 cc

Group C

- Received Inj. Bupivacaine 2.4 cc+
  Inj. Clonidine 30 µg=2.6 cc

PROCEDURE DETAILS:

On preoperative visit the patients were explained about the procedure details. Then preoperative baseline parameters like pulse rate, blood pressure, respiratory rate were recorded. Intravenous line started with 18 gauge intra venous cannula and preloaded with ringer's lactate 15 ml/kg 15min prior to subarachnoid blockade.

Following emergency drugs and equipments were kept ready before anaesthesia intervention.

- Boyles machine with oxygen cylinder
- Oxygen source
- Laryngoscope with various blades
- Airway in all sizes
- Suction apparatus
- Emergency drugs like ephedrine, dopamine, atropine and adrenaline

Patients were put in right lateral position and with strict aseptic precaution lumbar puncture was done with quincke standard 23 guage spinal needle.

After ensuing free flow of CSF, the drug was injected as per the group assigned.

The assigned amount of clonidine and normal saline were taken in 1 ml sterile tuberculine syringe.

After injection patient were put up in supine position. After attaining adequate peak level of sensory block, the surgeon was asked to proceed.

THE FOLLOWING PARAMETERS WERE RECORDED

1. Time of highest level of sensory block achieved by pin prick.
2. Onset and duration of motor blockade assessed by using bromage scale.
3. Pulse rate, Blood pressure, respiratory rate, spo_2 were monitored every 5 minutes for 30 minutes and every 1 5 minutes for next 90 min and then 30 min once for next 4 hours.
4. Any discomfort like nausea, vomiting, dry mouth and shivering are noted.
5. Hypotension is said to have occurred if the MAP falls less than 70 mm Hg and was treated with 100% O_2, Intravenous fluid bolus and Inj. Ephedrine in incremental doses.

6. Bradycardia (<60/min) – if present was treated with Inj. Atropine.
7. Sedation score was noted according to brain and ready scoring.
8. Post operative observation:
    a. Duration of procedure
    b. Two segment regression time (i.e. the time taken to decrease from maximum sensory level by two segments from initial level is noted)
    c. Duration of postoperative analgesia.
    d. Number of Inj.tramadol 100 mg ampoules required in first 24 hours.

SEDATION SCORE:

Brain and Ready sedation score was employed

0 - Fully awake

1 - Drowsy

2 - Drowsy but arousable on touch (or) call

3 - Drowsy but arousable on deep stimuli

4 - Somnolent

In the post operative period total duration of analgesia was taken as that period from time of subarachnoid block till patient requirement of analgesic medicine.

Pain was evaluated using **VISUAL ANALOG SCALE.**

0-1 - Excellent

2-4 - Good

5-6 - Fair

7-8 - Poor

9-10 - No relief

Pain score >5 supplementary analgesia given.

MOTOR BLOCK WAS ASSESSED BY BROMAGE SCALE

0 - Full flexion of knees, feet, able to lift the extended leg

1 - Unable to lift the extended leg. Just able to flex the knees and full flexion of feet possible

2 - Unable to flex the knees but flexion of feet possible.

3 - Unable to move the leg (or) feet

Also in the post operative period all patients were followed up for any complications like post operative nausea, vomiting, hypotension and respiratory depression, dry mouth.

Statistical significance was brought out by ANOVA table.

OBSERVATION AND RESULTS

In this randomized double blinded study conducted in 90 patients, the subjects were allocated in to three groups.

Group A - Inj. 0.5% Bupivacaine 2.4cc + 0.2 cc normal saline

Group B - Inj. 0.5% Bupivacaine 2.4cc+ 15 µg clonidine +0.1 cc normal saline

Group C Inj.0.5% Bupivacaine 2.4cc+ Inj. Clonidine 30µg

A. PROFILE OF CASES STUDIED

Table 1 : Age distribution

Age group	Cases in					
	Group A		Group B		Group C	
	No.	%	No.	%	No.	%
Upto 40 years	2	6.7	3	10	1	3.3
41-50years	10	33.3	12	40	11	36.7
51-60 years	14	46.7	12	40	12	40
>60years	4	13.3	3	10	6	20
Total	30	100	30	100	30	100
Range	39-64 yrs		39-66 yrs		39-69	
Mean	52.4		50.3		52.9	
S.D.	7		7.5		8.5	
'p'	0.4232 Not significant					

Age distribution in the group A ranges from 39 to 64 years with mean age of 52.4 years and standard deviation of 7.In group B the age distribution ranges from 39-66 years with mean age of 50.3 years and standard deviation of 7.5. In group C the age distribution ranges from 39 to 69 years with mean of 52.9 and standard deviation of 8.5

The p value for three groups are not significant, so the three groups are comparable.

Table 2: Height and weight

Variables	Group A		Group B		Group C		'p'
	mean	**S.D**	**mean**	**S.D**	**mean**	**S.D**	
Height(cms)	159.5	9.0	161.1	8.3	160.8	8.3	0.7984 not significant
Weight(kgs)	63.6	12.6	62.5	11.0	60.1	11.1	0.3413 not significant

In group A the mean height is 159.5 cm with standard deviation of 9
In group B the mean height is 161.1 cm with standard deviation of 8.3
In group C the mean height is 160.8 cm with standard deviation of 8.3

In group A the mean weight is 63.6 kg with standard deviation of 12.6
In group B the mean weight is 62.5 kg with standard deviation of 11
In group C the mean weight is 60.1 kg with standard deviation of 11.1

The p values for the height and weight of the three groups are not significant, so the three groups are comparable.

Table 3 : ASA status

ASA	Group A		Group B		Group C	
	No.	**%**	**No.**	**%**	**No.**	**%**
I	24	80	23	76.7	21	70
II	6	20	7	23.3	9	30
Total	30	100	30	100	30	100

In group A 80% belongs to ASA I and 20% ASA II

In group B 76.7% belongs to ASA I and 23.3% ASA II

In group C 70% belongs to ASAI and 30% ASA II

EFFICACY OF THE THREE GROUPS

Table 4 : Pulse rate

Pulse rate	Group-A		Group-B		Group-C	
	Mean	**S.D**	**mean**	**S.D**	**Mean**	**S.D**
Initial PR	88.3	9.5	85.6	9.8	84.9	11.3
Minimum PR	75.4	5.6	73.1	5.4	67.6	6.1
Average PR	82.5	5.9	80.8	6.3	73.6	5.3
Fall in PR	12.8	6.6	12.5	5.9	17.4	9.3
% fall in PR	14.1	6.1	14.2	5.4	19.6	8.6
'p' for 3 groups	0.0159 significant					
A&B	0.9058 not significant					
B&C	0.012 significant					
A&C	0.0141 significant					

In group A the initial mean pulse rate was 88.3 with standard deviation of 9.5 per minute, reaching a minimum of 75.4 with standard deviation of 5.6 per minute. The mean average pulse rate was 82.5 with standard deviation of 5.9 per minute and the percentage of fall in pulse rate was 14.1 with standard deviation of 6.1

In group B the initial mean pulse rate was 85.6 with standard deviation of 9.8 per minute, reaching a minimum of 73.1 with standard deviation of 5.4 per minute. The mean average pulse rate was 80.8 with standard deviation of 6.3 per minute and the percentage of fall in pulse rate was 14.2 with standard deviation of 5.4

In group C the initial mean pulse rate was 84.9 with standard deviation of 11.3 per minute, reaching a minimum of 67.6 with standard deviation of 6.1 per minute. The mean average pulse rate was 73.6 with standard deviation of 5.3 per minute and the percentage of fall in pulse rate was 19.6 with standard deviation of 8.6

Table 5: Mean Arterial Pressure

MAP	Group A		Group B		Group C	
	Mean	**S.D**	**Mean**	**S.D**	**mean**	**S.D**
Initial MAP	89.7	6.7	90.5	7.5	90.1	8.4
Minimum MAP	83.1	7.6	83.2	6.7	78.6	6.5
Average MAP	89.4	5.6	89.8	4.9	83.5	4.3
Fall in MAP	6.6	8.0	7.3	6.4	11.5	10.1
% fall in MAP	7.1	7.9	7.8	6.8	12.1	10
'p' for 3 groups	0.151 not significant					
A&B	0.2572 not significant					
B&C	0.0422 significant					
A&C	0.0347 significant					

In group A the initial mean arterial blood pressure was 89.7 with standard deviation of 6.7 mm Hg, reaching a mean minimum of 83.1with standard deviation of 7.6 mm Hg. The average was 89.4 with standard deviation of 5.6 mmHg. The percentage fall of 7.1 with standard deviation of 7.9 was noted.

In group B the initial mean arterial blood pressure was 90.5with standard deviation of 7.5 mm Hg, reaching a mean minimum of 83.2with standard deviation of 6.7 mm Hg. The average was 89.8 with standard deviation of 4.9 mmHg. The percentage fall of 7.8 with standard deviation of 6.8 was noted.

In group C the initial mean arterial blood pressure was 90.1 with standard deviation of 8.4mm Hg, reaching a mean minimum of 78.6with standard deviation of 6.5mm Hg. The average was 83.5 with standard deviation of 4.3 mmHg. The percentage fall of 12.1 with standard deviation of 10 was noted.

Table 6 : Medications

Medications	Group A		Group B		Group C	
	No.	**%**	**No.**	**%**	**No.**	**%**
Inj.ephedrine Given	3	10	2	6.7	4	13.3
Not given	27	90	28	93.3	26	86.7
Inj. Atropine Given	0	-	0	-	1	3.3
Not given	30	100	30	100	29	96.7

In group A 3 patients received inj. Ephedrine and no patients received inj. Atropine.

In group B 2 patients received inj. Ephedrine and no patients received inj. Atropine

In group C 4 patients received inj. Ephedrine and one patient received inj. Atropine.

Table 7: Sedation score

Sedation score	Group A		Group B		Group C	
	No.	**%**	**No.**	**%**	**No.**	**%**
0	30	100	26	86.7	12	40
1	-	-	4	13.3	18	60
2	-	-	-	-	-	-
Mean	0		0.13		0.6	
S.D	-		0.35		0.4983	
'p' for 3 groups	0.0001 significant					
A&B	0.0280 significant					
B&C	0.0001 significant					
A&C	0.0001 significant					

In group A sedation was observed in no patients

In group B grade I sedation score was observed in 4 patients

In group C grade I sedation score was observed in 18 patients .

Table 8: Respiratory rate & SpO2

	Respiratory rate			SpO2		
	Group A	**Group B**	**Group C**	**Group A**	**Group B**	**Group C**
Mean	14.9	14.8	14.7	99.7	99.5	99.6
S.D	1.2	1.1	0.8	0.55	0.68	0.67
"p" for 3 groups	0.5525 not significant			0.7827 not significant		
A&B	0.6894 not significant			0.4971 not significant		
B&C	0.5151 not significant			0.6309 not significant		
A&C	0.2736 not significant			0.8683 not significant		

In group A the mean respiratory rate was 14.9 with standard deviation of 1.2 and saturation of 99.7

In group B the mean respiratory rate was 14.8 with standard deviation of 1.1and saturation of 99.5

In group C the mean respiratory rate was 14.7with standard deviation of 0.8 and saturation of 99.6

Table 9 : Maximum sensory level

Max. SL	Group A		Group B		Group C	
	No.	**%**	**No.**	**%**	**No.**	**%**
T8	3	10	3	10	7	23.3
T9	13	43.3	5	16.7	9	30
T10	12	40	15	50	11	36.7
T11	2	6.7	7	23.3	3	10
Total	30	100	30	100	30	100

In group A the maximum sensory level of T8 , T9, T10, T11 was observed in 3, 13, 12,2 patients respectively.

In group B the maximum sensory level of T8 , T9, T10, T11 was observed in 3,5, 15,7 patients respectively.

In group C the maximum sensory level of T8 , T9, T10, T11 was observed in 7,9,11,3 patients respectively.

Table 10: Onset of max. sensory level

Onset SL	Group A	Group B	Group C
Mean	7.9	8.17	8.83
S.D	0.88	0.99	1.05
'p' 3 groups	0.0028 significant		
A&B	0.286 not significant		
B&C	0.0223 significant		
A&C	0.0008 significant		

In group A the onset of maximum sensory level occurs in 7.9 minutes with standard deviation of 0.88

In group B the onset of maximum sensory level occurs in 8.17 minutes with standard deviation of 0.99

In group C the onset of maximum sensory level occurs in 8.83minutes with standard deviation of 1.05

Table 11 : Two segment regression

2 segment regression	Group A	Group B	Group C
Mean	86.5	102.1	122.6
S.D	7.2	12.5	5.9
'p' 3 groups	0.0001 significant		
A&B	0.0001 significant		
B&C	0.0001 significant		
A&C	0.0001 significant		

In group A the two segment regression occurred in 86.5 minutes with standard deviation of 7.2

In group B the two segment regression occurred in 102.1 minutes with standard deviation of 12.5

In group C the two segment regression occurred in 122.6 minutes with standard deviation of 5.9

Table 12 : Motor onset

Motor onset	Group A	Group B	Group C
Mean	8.63	9.07	9.33
S.D	1.03	0.83	0.84
'p' 3 groups	0.029 significant		
A&B	0.0902 not significant		
B&C	0.2907 not significant		
A&C	0.0106 significant		

In group A the motor onset have occurred in 8.63 minutes with standard deviation of 1.03

In group B the motor onset have occurred in 9.07 minutes with standard deviation of 0.83

In group C the motor onset have occurred in 9.33 minutes with standard deviation of 0.84

Table 13 : Motor duration

Motor duration	Group A	Group B	Group C
Mean	110.9	125.2	142.7
S.D	9.9	9.5	8.5
'p' 3 groups	0.0001 significant		
A&B	0.0001 significant		
B&C	0.0001 significant		
A&C	0.0001 significant		

In group A mean motor duration was 110.9 minutes with standard deviation of 9.9

In group B mean motor duration was 125.2 minutes with standard deviation of 9.5

In group C mean motor duration was 142.7 minutes with standard deviation of 8.5

Table 14 : Duration of surgery (in minutes)

Duration of surgery(min)	Group A	Group B	Group C
Mean	95.7	95.8	97.6
S.D	14.8	9.7	10.7
'p' 3 groups	0.7104 not significant		
A&B	0.8355 not significant		
B&C	0.4812 not significant		
A&C	0.4814 not significant		

The mean duration of surgery was 95.7, 95.8, 97.6 minutes with standard deviation of 14.8, 9.7, 10.7 in group A, group B, group C respectively

Table 15 : Post operative analgesia (in minutes)

Post op analgesia(min)	Group A	Group B	Group C
Mean	175.9	194.9	272.2
S.D	11.6	22.0	33.2
'p' 3 groups	0.0001 significant		
A&B	0.0001 significant		
B&C	0.0001 significant		
A&C	0.0001 significant		

The post operative period till the patient demands systemic analgesic (ie. VAS score > 5) from the initiation of subarachnoid blockade.

In group A the mean duration of post operative analgesia was 175.9 minutes with standard deviation of 11.6

In group B the mean duration of post operative analgesia was 194.9 minutes with standard deviation of 22

In group C the mean duration of post operative analgesia was 272.2 minutes with standard deviation of 33.2

Table 16 : Number of tramadol(100mg) doses

No. of tramadol doses	Group A		Group B		Group C	
	No.	%	No.	%	No.	%
1	-	-	-	-	12	40
2	8	26.7	13	43.3	16	53.3
3	21	70	17	56.7	2	6.7
4	1	3.3	-	-	-	-
Mean	2.77		2.57		1.67	
S.D	0.5		0.5		0.61	
'p' 3 groups	0.0001 significant					
A&B	0.141 not significant					
B&C	0.0001 significant					
A&C	0.0001 significant					

In group A the mean requirement of 24 hour tramadol (100 mg) doses were 2, 3, 4 in 8, 21,1 patients respectively.

In group B the mean requirement of 24 hour tramadol (100 mg) doses were 2,3 in 13, 17 patients respectively.

In group C the mean requirement of 24 hour tramadol (100 mg) doses were 1,2,3 in 12,16,2 patients respectively

Table 17 : Complications

Complications	Group A		Group B		Group C	
	No.	%	No.	%	No.	%
Shivering	4	13.3	3	10	3	10
'p' A&B	0.5 not significant					
B&C	0.8 not significant					
A&C	0.5 not significant					

Shivering have occurred in 4 patients in group A and 3 patients in group B and 3 patients in group C.

Dry mouth have not been observed in any of the cases of in the three groups.

Nausea or vomiting have not been observed in any of the patients the three groups.

Statistical Tools :

The information collected regarding all the selected cases were recorded in a Master Chart. Data analysis was done with the help of computer using **Epidemiological Information Package (EPI 2008).**

Using this software range, frequencies, percentages, means, standard deviations, chi square and 'p' values were calculated. Kruskul Wallis chi-square test was used to test the significance of difference between quantitative variables and Yate's test for qualitative variables. A 'p' value less than 0.05 is taken to denote significant relationship.

DISCUSSION

The pain we perceive after a burn, bite (or) pinch is readily identifiable but difficult to define because it is differently perceived at different threshold.

Pain is defined as psychical adjunct of protective reflex – by Sherington in 1906.

The international association of society for pain (IASP) defined it as "An unpleasant sensory and emotional experience associated with actual (or) potential tissue damage (or) described in terms of such damage"

Clonidine assumes greater importance as anaesthetic adjuvant and analgesic. Its primary effect is sympatholytic. It reduces peripheral norepinephrine release by stimulation of prejunctional inhibitory alpha-2 adrenoreceptors. It inhibits central neural transmission in the dorsal horn by presynaptic and postsynaptic mechanism and directly in spinal preganglionic sympathetic neurons. Clonidine enhances both sensory and motor blockade of local anaesthetics in peripheral nerve and central neuraxial blockade. Clonidine blocks conduction of C and A gamma fibers and increases potassium conductance in isolated neurons and intensifies the conduction of local anesthetics.

By statistical analysis of three groups the age distribution was statistically not significant with a p value of 0.4232 (p> 0.05).

When comparing the height and weight of the patients in three groups it was statistically not significant with a p value of 0.7984 (p >0.05), 0.3413 (p>0.05) for height and weight respectively. All the three groups were comparable in relation to Age , height and Weight.

Duration of surgery was also comparable in all the three groups with a p value of 0.7104 (p> 0.05)

1. Post-operative analgesia was significantly prolonged in both the group B & C, but significantly much more in group C(30µg clonidine) .In group C , it was 272.2±33.2 minutes, while in group B it was 194.9±22 minutes, when compared to 175.9±11.6 minutes in group A. This is supported by sethi et al study where they have used 1µg per kg dose of clonidine with 12.5 mg of 0.5% bupivacaine and found that this dose prolongs the duration of post operative analgesia by 614 minutes in clonidine group .
2. 24 hours inj. Tramadol (100 mg) requirement is significantly reduced in group C cases. The mean number of dose requirement was 1.67 in group C, 2.57 in group B , when compared to 2.77 in group A. This finding is supported by sethi et al study where they had used inj.diclofenac as rescue analgesic and the 24 hours

requirement was 1.16 in clonidine group against 2.66 in control group.

3. Intra operative sedation was observed in group C but not of grade II or III or IV of brain and ready sedation score causing either respiratory depression or desaturation. This observation is supported by sethi et al study where they have observed sedation in 50 percent of their patients without significant respiratory depression or desaturation.

4. Hemodynamic changes:

   The fall in pulse rate was significant in three groups , but not less than 60 per min in group B or group C(except in one case) requiring inj. Atropine to treat it.

   The fall in mean arterial pressure was not significant in three groups and the requirement of inj. Ephedrine is similar in all groups . But in sethi et al study there was significant fall in mean arterial pressure though not requiring vasopressor treatment. Thus doses of 30µg and 15µg clonidine does not produce any change in mean arterial pressure values and is hemodynamically stable.

5. The two segment regression time was significantly prolonged in both the groups B and C, but more with group C. It was 122.6±5.9 minutes in group C ,102.1±12.5 minutes in group B and 86.5±7.2

minutes in group A. In sethi et al study also there was prolongation in two segment regression time of 218 minutes in clonidine 1µg per kg group.

6. The duration of motor blockade was significantly prolonged in both the groups B&C, but more with group C. The mean duration was 142.7 ±8.5 minutes in group C, 125.2±9.5 minutes in group B, and 110.9±9.9 minutes in group A . In sethi et al study the duration of motor blockade was 205 minutes in clonidine group.

7. The onset of maximum sensory blockade and the onset of motor blockade was significantly prolonged in group C when compared to other two groups. The onset of maximum sensory level was 8.83± 1.05, 8.17±0.99, 7.9±0.88 minutes in group C,B and A respectively. The duration of motor onset to achieve grade IV bromage scale was 9.33±0.84, 9.07±0.83, 8.63±1.03 minutes in group A,B and C respectively. This observation is supported by sethi et al study.

8. The side effects of clonidine like dry mouth was not observed in any of the cases of group B & C . While in sethi et al study they observed significant incidence of dry mouth with the dose of 1µg per kg clonidine group.

The study shows that adding clonidine 15µg and 30µg to bupivacaine significantly prolongs the duration of post operative analgesia when compared to bupivacaine alone without any side effects like dry mouth or hemodynamic instability. Adding 30µg of clonidine significantly results in more duration of post operative analgesia than adding 15µg of clonidine to bupivacaine.

SUMMARY

This is a randomized double blinded study conducted in 90 patients of ASA I and II undergoing elective inguinal hernia surgeries .Two different doses of clonidine 15 µg vs 30µg with spinal bupivacaine 2.4 ml was compared against 2.4 ml of bupivacaine alone.

Parameters observed were time of onset of sensory block and motor block, two segment regression time, duration of motor blockade, sedation score, duration of post operative analgesia and side effects.

1. The post op analgesia was significantly prolonged in group C and was 97 minutes more than the group A and 78 minutes more than group B.
2. The 24 hours analgesic requirements is significantly reduced in group C with 1.67 mean doses against 2.57 mean doses in group B and 2.77 mean doses in group A
3. Hemodynamicaly there was no significant fall in mean arterial pressure in group B and group C and the requirement of vasopressors was similar in all groups.
4. There was significant fall in pulse rate in group c, but not to such extent requiring treatment, (except in one case).
5. Sedation was observed in group C, producing good intra operative comfort to the patient. Neither respiratory depression nor desaturation was observed in any of the case of group C.

CONCLUSION

This study shows that adding clonidine 15µg and 30µg to bupivacaine significantly prolongs the duration of post operative analgesia when compared to bupivacaine alone in inguinal hernia surgeries. Adding 30µg of clonidine significantly results in more duration of post operative analgesia than adding 15µg of clonidine to bupivacaine without any side effects.

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PROFORMA

A COMPARATIVE STUDY OF TWO DOSES OF INTRATHECAL CLONIDINE WITH BUPIVACAINE IN INGUINAL HERNIA SURGERIES

AIM:

To assess the degree of post-op analgesia provided by 2 varying doses of clonidine with bupivacaine against bupivacaine alone in inguinal hernia surgeries.

NAME :

AGE/SEX :

IP.NO :

WARD/SU :

DATE :

ASA :

ANY MEDICAL ILLNESS :

PT. ON ANY DRUGS :

(tick any one)

GROUP-A : 0.5% BUP. 2.4 ml + 0.2 ml NS

GROUP-B : 0.5% BUP. 2.4 ml + 15 mics CLONIDINE + 0.1 ml NS

GROUP –C : 0.5%BUP. 2.4 ml + 30 mics CLONIDINE

TIME OF SAB:

PATIENT POSITION :

SPINAL NEEDLE- GAUGE :23 G

Time of SAB	Time to reach highest level of sensory blockade	Time to obtain grade IV motor block(bromagescale)	Time to reach 2- segment regression

Note : Time to be evaluated every 1 minute till it reach the target level

POST-OP ANALGESIA : by VAS scoring

Time to get first ANALGESIC DOSE

DURATON OF SURGERY :

Time	SPO2	RR	NIBP	PR	Any medications	Sedation score	Side effects
Pre-op							
SAB							
5 MIN							
1O m							
15 m							
20 m							
25 m							
30 m							
45 m							
1 hr							
1hr 15m							
1hr 30m							
2 hrs							
2.30 hrs							
3 hrs							
3.30 hrs							
4 hrs							
4.30 hrs							
5 hrs							
5.30 hrs 6 hrs							

MEDICATIONS : Inj. ATROPINE O.6mg i.v if PR< 60/min

If MAP < 70 mmHg ; rush IV FLUID

Inj. Ephedrine 3 mg (repeated if needed)

O2 supplementation, foot end elevation

SIDE- EFFECTS ; 1. shivering

2. nausea, retching, vomiting
3. sedation
4. dry mouth

OBSERVATIONS;

SENSORY BLOCKADE :

By pin prick every 5 min till it reaches the highest level

MOTOR BLOCKADE; (bromage scale) every 5 min till grade 4 is reached.

1- free movt. of legs / feet

2- just able to flex knees with free movt. of feet

3- unable to flex knees, but with free movt. of feet

4- unable to move legs/ feet

BELVILLE'S SCORE;

1- nausea; subjective unpleasant sensation with an urge to vomit

2- retching; laboured, spasmodic, rhythmic contraction of respiratory muscle

3- vomiting; retching with expulsion of gastric contents.

SHIVERING: (crossley & mahajan scoring)

1- pilo erection

2- contraction of any one muscle group

3- contraction of more than one muscle group

4- whole body shivering

SEDATION SCORE; (brain and ready scoring)

0- Fully awake

1- drowsy

2- drowsy but arousable to touch / call

3- drowsy but arousable on deep stimuli

4- somnolent

Pain was evaluated using **VISUAL ANALOG SCALE.**

0-1 - Excellent

2-4 - Good

5-6 - Fair

7-8 - Poor

9-10 - No relief

Pain score >5 – supplementary analgesia given

In the post operative period total duration of analgesia was taken as that period from time of subarachnoid block till patient requirement of analgesic (inj. Tramadol 100 mg).

Age in Years	Group A No.	%	Group B No.	%	Group C No.	%
Upto 40 years	2	6.7	3	10	1	3.3
41-50years	10	33.3	12	40	11	36.7
51-60 years	14	46.7	12	40	12	40
>60years	4	13.3	3	10	6	20

Group A	30
Group B	30
Group C	30

ASA	Group A		Group B		Group C	
	No.	**%**	**No.**	**%**	**No.**	**%**
I	24	80	23	76.7	21	70
II	6	20	7	23.3	9	30

medications	**Group A**		**Group B**		**Group C**	
	No.	**%**	**No.**	**%**	**No.**	**%**
Inj.ephedrine Given	3	10	2	6.7	4	13.3
Not given	27	90	28	93.3	26	86.7
Inj. Atropine Given	0	0	0	0	1	3.3
Not given	30	100	30	100	29	96.7

medications	**Group A**		**Group B**		**Group C**	
	No.	**%**	**No.**	**%**	**No.**	**%**
Inj. Epidrine Given	3	10	2	6.7	4	13.3
Not given	27	90	28	93.3	26	86.7
Inj. Atropine Given	0	0	0	0	1	3.3
Not given	30	100	30	100	29	96.7

Sedation score	Group A		Group B		Group C	
	No.	%	No.	%	No.	%
0	30	100	26	86.7	12	40
1	0	0	4	13.3	12	40
2	0	0	0	0	6	20

Group A	14.1
Group B	14.2
Group C	19.6

Group A	7.1
Group B	7.8
Group C	12.1

Group A	0.1
Group B	0.13
Group C	0.8

Max. SL	Gr-A		Gr-B		Gr-C	
	No.	%	No.	%	No.	%
T8	3	10	3	10	7	23.3
T9	13	43.3	5	16.7	9	30
T10	12	40	15	50	11	36.7
T11	2	6.7	7	23.3	3	10

Group A	7.9
Group B	8.17
Group C	8.83

Group A	86.5
Group B	102.1
Group C	122.6

Group A	175.9
Group B	194.9
Group C	272.2

Group A	110.9
Group B	125.2
Group C	142.7

Group A	8.63
Group B	9.07
Group C	9.33

Group A	2.77
Group B	2.57
Group C	1.67

s.no	IP.no	group	age	sex	ht	wt	ASA	PR-initial	PR-min	PR-avg.	MAP-initial	MAP-min	MAP-avg	eped.	atropin	sedation	RR	SpO2	max. -SL	onset-SI(min)	2 SR	M- onset	M-duration	duration-surgery	dry mouth	shivering	post-op analgesia	no. of tramadol
1	42967	A	45	M	148	36	I	96	78	82	87	83	89	0	0	0	16	99	T10	8m	94m	10m	112	96	no	no	184m	3
2	39836	A	55	M	156	46	I	106	89	94	89	85	91	0	0	0	14	100	T9	7m	88m	8m	122	104	no	no	166m	2
3	44478	A	49	M	163	74	I	89	79	82	96	92	98	0	0	0	16	99	T9	8m	92m	9m	126	90	no	no	190m	3
4	44219	A	40	M	148	82	I	78	74	82	97	91	89	0	0	0	15	100	T10	10m	84m	10m	118	78	no	no	170m	3
5	44039	A	56	M	162	86	I	86	76	79	79	79	83	0	0	0	15	100	T8	7m	98m	8m	126	106	no	no	202m	3
6	44676	A	60	M	168	58	I	92	70	84	87	83	89	0	0	0	16	100	T9	9m	88m	10m	118	98	no	yes	160m	3
7	44181	A	62	M	162	62	I	97	83	89	93	89	96	0	0	0	13	100	T10	7m	80m	8m	102	90	no	no	170m	3
8	46874	A	48	M	158	68	I	76	70	71	83	79	82	0	0	0	12	99	T9	8m	94m	8m	110	78	no	no	190m	2
9	46864	A	52	M	155	48	I	68	65	76	87	83	89	0	0	0	14	100	T9	8m	78m	9m	96	96	no	no	174m	3
10	46570	A	54	M	171	64	I	89	84	83	93	93	97	0	0	0	15	99	T8	7m	88m	8m	94	102	no	no	168m	2
11	44412	A	64	M	172	72	II	91	72	81	103	69	93	1	0	0	16	99	T8	9m	92m	9m	112	98	no	no	156m	3
12	48861	A	58	M	168	78	I	79	69	84	93	86	89	0	0	0	13	100	T9	8m	98m	9m	122	120	no	yes	194m	2
13	45866	A	60	M	156	58	I	88	72	77	79	67	77	1	0	0	14	100	T10	7m	74m	8m	98	102	no	no	188m	3
14	48846	A	53	I	149	53	II	93	75	83	88	83	91	0	0	0	14	100	T10	9m	86m	9m	102	114	no	no	176m	3
15	46969	A	49	M	145	47	I	76	69	71	97	93	98	0	0	0	15	100	T9	8m	88m	8m	104	126	no	no	170m	3
16	47879	A	42	M	166	38	I	84	74	77	101	66	93	1	0	0	15	100	T10	7m	78m	7m	106	120	no	no	190m	2
17	48505	A	47	M	173	66	I	78	71	73	83	79	85	0	0	0	14	100	T11	9m	76m	10m	112	80	no	yes	166m	3
18	48510	A	56	M	148	63	I	96	75	83	93	93	97	0	0	0	15	99	T11	7m	78m	10m	124	70	no	no	158m	3
19	48534	A	59	M	172	59	I	81	71	92	97	91	96	0	0	0	16	100	T9	8m	90m	8m	126	88	no	no	182m	3
20	47070	A	48	M	149	56	II	87	80	81	92	83	89	0	0	0	17	100	T10	7m	80m	7m	114	90	no	no	176m	3
21	47721	A	52	M	167	64	I	94	79	83	77	75	81	0	0	0	15	100	T10	9m	78m	10m	96	102	no	yes	180m	3
22	46193	A	42	M	153	62	I	104	76	89	83	79	84	0	0	0	16	100	T10	9m	96m	10m	120	92	no	no	170m	2
23	48965	A	39	M	158	86	I	97	83	91	89	81	87	0	0	0	15	100	T10	7m	92m	8m	114	88	no	no	182m	2
24	48327	A	48	M	148	78	I	106	80	89	93	93	97	0	0	0	14	98	T10	8m	80m	9m	102	82	no	no	166m	3
25	47764	A	51	M	163	64	II	89	81	92	91	85	89	0	0	0	15	100	T9	7m	84m	7m	106	78	no	no	170m	3
26	106976	A	62	M	169	73	I	72	66	81	89	81	87	0	0	0	16	99	T9	8m	90m	8m	114	70	no	no	160m	4
27	103113	A	46	M	172	64	II	88	73	82	79	75	81	0	0	0	13	99	T9	9m	84m	10m	102	96	no	no	176m	3
28	106959	A	62	M	155	66	I	87	80	82	87	81	86	0	0	0	15	100	T9	7m	78m	7m	98	120	no	no	170m	3

29	1839	A	54	M	149	68	II	89	76	79	89	84	87	0	0	0	16	100	T10	8m	92m	9m	114	106	no	no	190m	2
30	1688	A	58	M	162	70	I	92	73	83	97	91	93	0	0	0	16	100	T9	7m	96m	8m	116	90	no	no	182m	3
31	1680	B	44	M	142	39	I	107	82	91	89	79	87	0	0	0	14	100	T10	7m	106m	8m	132	96	no	no	206m	2
32	3718	B	48	M	148	44	II	97	79	89	91	83	89	0	0	0	15	98	T9	8m	96m	9m	118	110	no	no	186m	3
33	3999	B	52	M	156	48	I	73	65	79	93	87	91	0	0	0	16	99	T8	9m	102m	10m	132	90	no	no	110m	2
34	4826	B	56	M	167	49	I	87	72	79	97	91	96	0	0	0	14	99	T11	8m	90m	8m	116	88	no	no	170m	3
35	48918	B	58	M	168	50	II	97	74	85	79	79	83	0	0	0	15	99	T10	7m	86m	8m	128	76	no	no	202m	3
36	96416	B	59	M	166	54	I	77	67	71	83	81	85	0	0	0	16	99	T11	9m	110m	7m	128	90	no	no	180m	2
37	99372	B	66	M	169	57	I	73	65	82	87	83	89	0	0	0	14	99	T10	7m	122m	8m	136	98	no	no	210m	2
38	99189	B	62	M	174	52	I	86	75	81	101	93	97	0	0	1	15	100	T10	8m	88m	9m	102	102	no	yes	214m	3
39	99861	B	55	M	173	66	II	92	80	87	103	87	93	0	0	0	13	100	T9	9m	96m	10m	118	116	no	no	196m	2
40	98104	B	45	M	166	67	I	88	79	83	97	89	95	0	0	0	12	100	T8	7m	106m	9m	132	98	no	no	188m	2
41	98976	B	40	M	168	64	I	78	72	73	79	77	81	0	0	0	15	100	T10	8m	108m	10m	128	88	no	no	192m	3
42	98972	B	39	M	146	63	II	93	73	84	83	83	86	0	0	0	16	100	T11	9m	109m	10m	126	92	no	no	178m	3
43	99810	B	43	M	154	69	I	97	72	85	87	81	86	0	0	0	17	100	T10	7m	114m	9m	134	92	no	no	192m	3
44	101981	B	56	M	156	77	I	104	84	91	93	79	89	0	0	0	15	100	T9	8m	112m	9m	131	88	no	no	194m	2
45	161596	B	43	M	152	78	I	79	70	88	97	89	93	0	0	1	16	100	T10	9m	92m	10m	108	86	no	yes	196m	2
46	101700	B	47	M	163	73	II	83	73	77	92	67	91	1	0	0	14	99	T8	9m	96m	9m	118	82	no	no	211m	3
47	98867	B	39	M	166	72	I	97	82	85	101	93	97	0	0	0	14	99	T11	10m	98m	10m	122	98	no	no	212m	2
48	99760	B	41	M	163	67	I	77	70	74	103	87	95	0	0	0	15	98	T10	7m	94m	9m	128	102	no	no	214m	3
49	101745	B	42	M	169	64	I	69	64	77	77	77	81	0	0	0	14	100	T11	9m	102m	10m	124	114	no	no	240m	3
50	100640	B	47	M	147	56	I	78	67	68	83	79	84	0	0	1	14	100	T10	9m	106m	10m	122	92	no	no	210m	2
51	104134	B	48	M	156	53	I	74	66	71	86	81	87	0	0	0	14	100	T10	8m	104m	8m	128	104	no	no	180m	3
52	103113	B	51	M	158	59	II	79	68	73	89	83	91	0	0	0	15	100	T9	7m	116m	9m	142	106	no	no	176m	3
53	28285	B	52	M	160	60	I	86	72	79	91	66	93	1	0	0	15	100	T10	9m	118m	9m	138	92	no	no	180m	2
54	30162	B	56	M	166	73	II	89	74	81	93	91	93	0	0	0	16	100	T11	10m	114m	10m	132	78	no	no	190m	2
55	30756	B	48	M	162	79	I	93	76	87	97	91	96	0	0	0	14	100	T10	8m	104m	9m	128	96	no	no	196m	3
56	30734	B	47	M	167	85	I	88	72	79	93	87	91	0	0	0	15	100	T9	9m	108m	9m	124	102	no	yes	202m	2
57	6568	B	56	M	168	66	I	91	80	87	99	91	97	0	0	1	16	99	T10	9m	68m	10m	102	104	no	no	214m	3
58	6613	B	52	M	157	68	I	77	75	75	83	83	87	0	0	0	14	98	T11	7m	74m	9m	122	92	no	no	202m	3
59	6215	B	64	M	159	57	I	78	71	86	81	79	83	0	0	0	15	100	T10	7m	110m	8m	126	96	no	no	214m	3
60	4378	B	52	M	166	66	I	81	74	77	89	81	87	0	0	0	16	100	T10	7m	114m	9m	132	106	no	no	192m	3

61	6668	C	45	M	142	38	I	106	71	77	86	77	83	0	0	1	14	100	T9	9m	126m	10m	148	96	no	no	222m	2
62	5014	C	46	M	147	45	I	109	73	76	79	76	81	0	0	1	15	99	T8	10m	120m	10m	152	110	no	no	246m	3
63	6601	C	48	M	155	49	I	79	62	67	94	86	89	0	0	0	16	98	T10	11m	130m	11m	160	80	no	no	262m	2
64	7842	C	55	M	166	50	I	89	67	73	97	79	81	0	0	1	14	99	T8	9m	132m	9m	158	78	no	no	242m	1
65	20270	C	56	M	172	55	I	92	75	78	99	83	85	0	0	0	14	100	T9	10m	110m	10m	130	94	no	no	276m	1
66	9899	C	54	M	173	56	I	70	63	66	101	74	79	0	0	0	15	100	T8	11m	120m	11m	136	96	no	no	278m	2
67	20366	C	66	M	148	58	II	76	64	69	104	77	83	0	0	1	16	100	T10	8m	126m	9m	146	84	no	no	322m	1
68	6590	C	73	M	155	65	I	83	69	74	91	67	79	1	0	1	14	100	T9	9m	118m	10m	130	92	no	no	284m	1
69	8476	C	67	M	167	68	II	96	73	79	77	74	79	0	0	1	15	100	T8	7m	130m	8m	142	114	no	no	286m	1
70	8490	C	54	M	163	70	I	79	71	73	81	79	83	0	0	1	14	99	T9	8m	118m	9m	144	110	no	no	284m	1
71	21665	C	53	M	168	84	I	83	73	76	85	83	86	0	0	0	15	100	T8	9m	128m	10m	146	98	no	no	266m	2
72	24717	C	44	M	169	56	I	69	61	73	93	89	91	0	0	0	14	100	T9	10m	124m	10m	142	106	no	no	256m	2
73	24388	C	39	M	170	57	II	78	69	73	97	79	81	0	0	1	14	99	T10	9m	126m	10m	142	110	no	no	196m	2
74	21152	C	45	M	172	53	I	82	71	74	77	74	79	0	0	0	15	98	T11	8m	130m	9m	152	88	no	no	296m	2
75	27282	C	42	M	155	66	I	87	69	73	103	91	93	0	0	1	13	99	T10	9m	134m	10m	148	78	no	no	292m	1
76	26433	C	46	M	158	69	II	91	52	79	101	68	77	1	1	1	15	100	T9	8m	132m	9m	150	102	no	no	291m	1
77	27986	C	47	M	167	82	I	97	71	79	88	77	81	0	0	1	14	100	T10	7m	120m	8m	142	114	no	no	284m	2
78	27982	C	55	M	166	64	II	102	77	82	83	81	85	0	0	1	15	100	T11	9m	118m	9m	130	90	no	no	296m	2
79	26392	C	42	M	156	84	I	88	68	73	89	83	87	0	0	0	15	100	T8	10m	122m	10m	142	96	no	yes	288m	2
80	28882	C	46	M	169	44	II	91	66	70	93	86	89	0	0	1	16	100	T9	9m	124m	9m	146	86	no	no	294m	1
81	28013	C	52	M	163	48	II	97	67	71	77	73	79	0	0	0	15	100	T10	8m	116m	8m	138	98	no	no	326m	1
82	41456	C	53	M	167	66	I	79	69	73	96	83	86	0	0	0	14	100	T11	10m	118m	10m	142	110	no	no	312m	1
83	40148	C	60	M	155	64	I	69	61	63	91	79	81	0	0	0	15	99	T9	9m	114m	9m	128	106	no	no	318m	1
84	30500	C	67	M	158	56	I	72	64	69	83	81	85	0	0	1	15	98	T8	8m	120m	9m	136	104	no	yes	241m	2
85	32348	C	61	M	154	58	I	66	60	62	91	65	77	1	0	1	16	100	T10	8m	124m	9m	142	114	no	no	186m	3
86	38853	C	62	M	149	67	II	93	74	79	101	67	81	1	0	1	14	100	T10	9m	122m	9m	148	102	no	no	262m	2
87	39659	C	55	M	166	62	I	77	54	82	97	86	89	0	0	0	15	100	T10	7m	116m	8m	126	96	no	no	276m	2
88	36722	C	57	M	155	54	I	76	66	69	79	78	81	0	0	0	14	100	T10	8m	118m	8m	138	92	no	yes	268m	2
89	40789	C	52	M	158	58	II	79	69	73	83	79	85	0	0	1	14	100	T9	9m	122m	10m	146	94	no	no	271m	2
90	43009	C	46	M	160	56	I	93	78	83	87	85	89	0	0	1	15	100	T10	9m	120m	9m	152	90	no	no	244m	2